PMDA
No.11 October 2023

ORANGE Letter

< Rapid announcement of Inspectional Observations >

** Observed Regulatory Attention / Notification of GMP Elements*

Communication within the Organization (From Management to the Manufacturing Floor)

≪ Related GMP Ministerial Ordinance** Clause: Article 3-3 ≫

** GMP Ministerial Ordinance: Ministerial Ordinance on Standards for Manufacturing Control and Quality Control for Drugs and Quasi-drugs(MHLW Ministerial Ordinance No. 179 dated December 24, 2004)

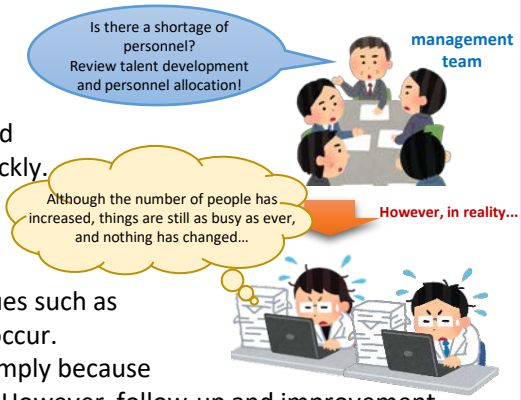
Observation Management was not aware of the status of improvements at the manufacturing floor.

< Background >

- The GMP Ministerial Ordinance stipulates the following requirements for the pharmaceutical quality system (PQS):
  1. To establish an effective PQS.
  2. To allocate the necessary resources[1] to establish the Quality Policy, which serves as the fundamental policy for ensuring product quality, and to achieve the Quality Objectives established at the manufacturing site based on the policy.
  3. To periodically review the PQS and take necessary actions based on the results.
- The manufacturing site manufactures more than 50 non-sterile drug products.

1) refers to those to be utilized for manufacturing control and quality control at the manufacturing site, such as individual knowledge and skill, technique, equipment, etc.

< Observed situation >



- During a management review, it was reported that quality testing had not been carried out due to a shortage of personnel and insufficient training. In response, the management team instructed that talent development and personnel allocation be reviewed quickly.
- Although several personnel were subsequently recruited, the increase in workload, including the training required for the new hires, was not adequately addressed, and an appropriate review of personnel allocation was not carried out. As a result, issues such as deviation caused by inadequate resource allocation continued to occur.
- The management team judged that the issue had been resolved simply because the number of personnel at the manufacturing site had increased. However, follow-up and improvement instructions after the management review were insufficient, and the issue remained un addressed.

< Possible problems and risks >

- If the improvement cycle for resolving problems is not functioning effectively, products of required quality may not be consistently supplied to the market. In such cases, the pharmaceutical company may fail to fulfill its responsibility to ensure a stable supply of medicines.

Check Points

(observed at a biological product manufacturing site in Japan)

- ☐ Is the workload concentrated on specific personnel, resulting in delays in necessary tasks and potential dysfunction of the PQS?
- ☐ Are the improvement measures based on the results of the management review realistic, and have actionable plans been established to ensure their implementation?
- ☐ Has the management team confirmed that the pharmaceutical quality system is functioning effectively as a result of the improvement measures being implemented?

Is management receiving accurate information from the manufacturing floor?

- ✓ After issuing improvement instructions, management should continue to monitor the implementation of improvements at the manufacturing site. If no improvements are observed, they should consider not only human resource measures (e.g., staffing or reallocation), but also multifaceted approaches such as system-based improvements to enhance operational efficiency.
- ✓ In particular, for issues that require immediate action at the manufacturing site, it is important for management to take a proactive approach by actively following up on field information, rather than taking a passive approach and waiting for reports.
- ✓ While it is not necessary for management to grasp all information, it is desirable to establish reporting structures and systems that enable access to accurate and unfiltered information from the manufacturing site.